

**Claims****What is claimed is:**

1. A composition comprising an EGF receptor agonist and L-arginine, a bioequivalent of L-arginine,  
4 or an NO-donor wherein the ratio of the agonist and L-arginine, bioequivalent thereof, or NO-donor is between 1:45,000,000 and 1:4,500 (mole:mole), or between 1:20,000,000 and 1:100,000, or between 1:10,000,000 and 1:1,000,000, or between 1:4,700,000 and 1:47,000.
2. The composition of claim 1 in solid form.
- 8 3. The composition of claim 1 or 2 in lyophilized form.
4. The composition of claim 1 in solution form.
5. The composition of claim 4, wherein the solution is suitable for oral delivery to a human.
6. The composition of claim 4, wherein the solution is suitable for enteral delivery to a human.
- 12 7. The composition of any of claims 1 to 6, wherein the EGF receptor agonist is EGF.
8. The composition of claim 7, wherein the EGF receptor agonist is synthetic, optionally manufactured by chemical synthesis or recombinantly, or derived from natural sources.
9. The composition of any of claims 1 to 8, for the treatment of necrotizing enterocolitis.
- 16 10. A unit dose comprising L-arginine, bioequivalent thereof, or an NO-donor and an EGF receptor agonist suitable for the oral administration to an animal upon dissolution with a pharmaceutically acceptable liquid.
11. The unit dose of claim 10, wherein the pharmaceutically acceptable liquid is selected from the  
20 group consisting of water, saline, infant formula, buffered solution, expressed breast milk, other suitable carriers, and combinations thereof.
12. The unit dose of claim 10 or 11, comprising L-arginine in a quantity of from about 200 mg/kg/day (0.9 mmol/kg/day) to about 500 mg/kg/day (2.4 mmol/kg/day), or more preferably from about 250  
24 mg/kg/day (1.2 mmol/kg/day) to about 400 mg/kg/day (1.9 mmol/kg/day), or more preferably from about 300 mg/kg/day (1.4 mmol/kg/day) to about 350 mg/kg/day (1.6 mmol/kg/day).

13. The unit dose of claims 10, 11, or 12, wherein the EGF receptor agonist is supplied in a quantity of 0.032 nmol/kg/day to about 0.32  $\mu$ mol/kg/day, or more preferably from about 0.16 nmol/kg/day to about 0.16 mmol/kg/day, or more preferably from about 0.32 nmol/kg/day to about 32 nmol/kg/day.
- 4 14. The unit dose of any of claim 10, 11, 12, or 13, wherein the EGF receptor agonist is EGF.
15. The unit dose of any of claim 10, 11, 12, 13, or 14, wherein the animal is a human infant.
16. The unit dose of claim 15 wherein the human infant is premature.
- 8 17. A unit dose comprising L-arginine, a bioequivalent thereof, or an NO-donor and an EGF receptor agonist suitable for the intravenous administration to a human infant, optionally upon dissolution with a pharmaceutically suitable solution.
18. The unit dose of claim 17, wherein the pharmaceutically acceptable solution is saline or a buffered solution.
- 12 19. The unit dose of claims 17 or 18, wherein the ratio of the agonist and L-arginine, bioequivalent thereof, or NO-donor is between 1:45,000,000 and 1:4,500 (mole:mole), or between 1:20,000,000 and 1:100,000, or between 1:10,000,000 and 1:1,000,000, or between 1:4,700,000 and 1:47,000.
20. The unit dose of any of claims 17, 18, or 19, wherein the EGF receptor agonist is EGF.
- 16 21. The unit dose of any of claim 17, 18, 19, or 20, wherein the animal is a human infant.
22. The unit dose of claim 21 wherein the human infant is premature.
23. A method of treating necrotizing enterocolitis in an animal, the method comprising administering an EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor to the animal.
- 20 24. A method of prophylaxis of necrotizing enterocolitis in an animal, the method comprising administering an EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor to the animal at risk for necrotizing enterocolitis.
- 24 25. The method of claim 24 wherein the animal is an infant, particularly an infant suffering from cardiovascular disturbances, or a premature infant at an age prior to normal term.
26. The method of claim 25 wherein the animal is a human infant having a weight of less than or equal to about 1700 g, or less than about 1400 g, more preferably less than about 1300 g, more preferably less than about 1200 g, more preferably less than about 1100 g, more preferably less than

about 1000 g, more preferably less than about 900 g, more preferably less than about 800 g, more preferably less than about 750 g.

4 27. A method of treating necrotizing enterocolitis or of prophylaxis of necrotizing enterocolitis in a premature infant, the method comprising enterally administering to the infant an EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor.

28. The method of claim 27, wherein the EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor are administered together in a mixture.

8 29. The method of claim 28, wherein the mixture is administered at least once daily.

30. The method of any of claims 27 to 29, wherein the EGF receptor agonist is EGF.

31. The method of claim 30, wherein the EGF is synthesized recombinantly.

12 32. A kit comprising therapeutic amounts of an EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor, and instructions for use in the treatment of a medical disorder.

33. The kit of claim 32, wherein the medical disorder is necrotizing enterocolitis.

34. The kit of claim 32, wherein the agonist and L-arginine, a bioequivalent thereof, or NO-donor are supplied combined in solid form.

16 35. The kit of claim 34, wherein the instructions include the step of dissolving the solid form in a solution suitable for oral administration.

36. The kit of claim 34, wherein the instructions include the step of dissolving the solid form in a solution suitable for intravenous administration.

20 37. The kit of claim 34, wherein the agonist and L-arginine, a bioequivalent thereof, or an NO-donor are supplied separately.

38. The kit of claim 37, wherein at least one of the agonist and L-arginine, a bioequivalent thereof, or NO-donor is in solid form.

24 39. The kit of claim 37, wherein at least one of the agonist and L-arginine, a bioequivalent thereof, or NO-donor is in solution.

40. The kit of any of claims 37 to 39, wherein the instructions include a step of mixing the agonist and L-arginine, a bioequivalent thereof, or an NO-donor before administration.

41. A method of treating NEC in an animal comprising delivering an EGF receptor agonist to the  
4 intestinal tract of the animal and increasing the *in vivo* generation of NO within the intestinal tract of the animal.

42. The method of claim 41, wherein increasing the *in vivo* generation of NO includes administering a substrate of nitric oxide synthase, or a bioequivalent of the substrate, to the animal.

8 43. The method of claim 41, wherein increasing the *in vivo* generation of NO includes administering an NO-donor.

44. A method of treating a person, optionally an infant, at risk of NEC comprising delivering an EGF receptor agonist to the intestinal tract of the patient and increasing the *in vivo* generation of NO within  
12 the intestinal tract of the person.

45. The method of claim 44, wherein increasing the *in vivo* generation of NO includes administering a substrate of nitric oxide synthase, or a bioequivalent of the substrate, to the person.

46. The method of claim 44, wherein increasing the *in vivo* generation of NO includes administering  
16 an NO-donor.

47. Use of an EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor for treating necrotizing enterocolitis in an animal.

48. The use of claim 47 wherein the animal is an infant, particularly an infant suffering from  
20 cardiovascular disturbances, or a premature infant at an age prior to normal term.

49. The use of claim 48 wherein the animal is a human infant having a weight of less than or equal to about 1700 g, or less than about 1400 g, more preferably less than about 1300 g, more preferably less than about 1200 g, more preferably less than about 1100 g, more preferably less than about 1000 g,  
24 more preferably less than about 900 g, more preferably less than about 800 g, more preferably less than about 750 g.

50. Use of an EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor for treating necrotizing enterocolitis or of prophylaxis of necrotizing enterocolitis in a premature infant.

51. The use of any of claims 47 to 50, wherein the EGF receptor agonist and L-arginine, a bioequivalent thereof, or an NO-donor are administered together in a mixture.
52. The use of claim 57, wherein the mixture is administered at least once daily.
- 4 53. The use of any of claims 47 to 52, wherein the EGF receptor agonist is EGF.
54. The use of claim 53, wherein the EGF is synthesized recombinantly.
55. Use of an EGF receptor agonist and a second component, the second component capable of increasing the *in vivo* generation of NO within the intestinal tract of the animal, for treating NEC in an  
8 animal.
56. The use of claim 55, wherein the second component is a substrate of nitric oxide synthase, or a bioequivalent of the substrate.
57. The use of claim 55, wherein the second component is an NO-donor.
- 12 58. Use of an EGF receptor agonist and a second component, the second component capable of increasing the *in vivo* generation of NO within the intestinal tract of a person, for treating a person, optionally an infant at risk of NEC.
59. The use of claim 58, wherein the second component is a substrate of nitric oxide synthase, or a  
16 bioequivalent of the substrate.
60. The use of claim 58, wherein the second component is an NO-donor.